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wherein

R⁵, R⁶, R⁷ and R⁸ are independently selected from the group consisting of H, halogen, CF₃, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)

C₆)alkylamino, di(C₁-C₄)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-

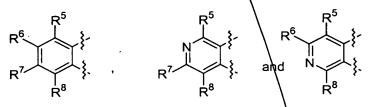
C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, cyano, nitro, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₁-C₆)alkoxycarbonyl,

(C₁-C₆)alkoxycarbonyl (C₁-C₆)alkyl, CONH₂, CO-NH-(C₁-C₆)alkyl, CO-N[(C₁-C₆)alkyl]₂, SO₂NH₂, SO₂NH-(C₁-C₆)alkyl, SO₂N-[(C₁-C₆)alkyl]₂ and (C₁-C₆)heteroalkoxy; or two adjacent R groups selected from R⁵, R⁶,

 R^7 and R^8 , can be linked together to form a new 5- or 6-membered

carbocyclic or heterocyclic ring.

13. A compound of claim 12, wherein W is N; X is CH; Y is O or S; and A is selected from the group consisting of:



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- 14. A compound of claim 1, wherein B contains a nitrogen atom at a position two atoms away from the atom attaching B to the remainder of the molecule.
- 1 15. A compound of claim 1, wherein B contains a nitrogen atom at the point of attachment of B to the remainder of the molecule.
 - 16. A compound of claim 1, wherein B is selected from the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-

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3	1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-
4	triazolyl, and 4-methyl-1,2,4-triazol-3-yl.

- A compound of claim 1, wherein B is selected from the group 1 2 consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted 3 thiazolyl and substituted or unsubstituted triazolyl.
- 1 18. A compound of claim 13, wherein B contains a nitrogen atom at a 2 position two atoms away from the atom attaching B to the remainder of the molecule.
- 1 19. A compound of claim 13, wherein B contains a nitrogen atom at 2 the point of attachment of B to the remainder of the molecule.
 - 20. A compound of claim 13, wherein B is selected from the group consisting of 1-methylimidazol, 5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-1-yl, 5-(trifluoromethyl)imidazol 1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4triazolyl, and 4-methyl-1,2,4-triazòl-3-yl.
 - 21. A compound of claim 13, wherein B is selected from the group consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted thiazolyl and substituted or unsubstituted triazolyl.
- A compound of claim, 1, wherein W is N; X is CH; Y is O or S; Z 22. is H, CH₃, NH₂ or NHCH₃; R¹ is H, (C₁-C₆)alkyl, (C₁-C₁₀)heteroalkyl, (C₄-2
 - C₁₀)cycloheteroalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, aryl(C₁-C₄)alkyl, aryl(C₁-3
 - C_4)heteroalkyl, heteroaryl(C_1 - C_4)alkyl, heteroaryl(C_1 - C_4)heteroalkyl, or perfluoro(C_1 -4
 - C₆)alkyl; R⁴ is H; A represents 5

- wherein R⁶ and R⁷ are independently selected from the group consisting of 7 H, halogen, CF_3 , CF_3O , (C_1-C_4) alkyl, (C_2-C_4) alkenyl, (C_2-C_4) alkynyl, (C_1-C_4) heteroalkyl, 8 (C₃-C₁₀)cycloheteroalkyl-alkyl and cyano; and B is a five-membered aromatic ring 9
- 10 system containing at least one nitrogen atom.
 - A compound of claim 22, wherein Y is S. 23.

	1	24. A compound of claim 22, wherein Z is NR ² R ³ .
	1	A compound of claim 22, wherein Z is NH ₂ .
	1	26. A compound of claim 22, wherein R^1 is (C_1-C_6) alkyl, (C_1-C_6)
	2	C ₆)heteroalkyl or (C ₃ -C ₁₀)cycloheteroalkyl-alkyl.
h	1	27. A compound of claim 22, wherein B is a five-membered aromatic
<i>U</i> U	2	ring system containing 1-2 nitrogen atoms and 0-1 sulfur atoms.
Al		
	1	28. A compound of claim 27, wherein B is unsubstituted or substituted
	2	by (C ₁ -C ₃)alkyl, CF ₃ , cyano, or halogen.
	<u>ļ.</u> 1	29. A compound of claim 22, wherein Z is NH ₂ ; R ⁶ is selected from the
	•	group consisting of H, halogen, CF ₃ , CF ₃ O, (C ₁ -C ₄)alkyl, (C ₂ -C ₄)alkenyl, (C ₁ -
	2 3 4	C ₄)heteroalkyl, (C ₃ -C ₁₀)cycloheteroalkyl-alkyl and cyano, wherein the alkyl, alkenyl and
	- 4 111 4	heteroalkyl groups optionally bear additional substituents selected from cyano,
	19 10 14	carboxamido,(C ₁ -C ₃)alkylsulfonyl or (C ₁ -C ₃)alkoxy; and R is selected from the group
	∗ું 6	consisting of H, halogen, CF ₃ , CF ₃ O, (C ₁ -C ₄)alkyl, (C ₂ -C ₄)alkenyl, (C ₂ -C ₄)alkynyl, (C ₁ -
		C ₄)heteroalkyl and cyano.
	o '	C4/inclorounkyr und Cyuno.
	7	30. A compound of claim 29, wherein R ⁶ is selected from the group
	1	consisting of CH ₂ (CH ₂) _m CN, CH ₂ (CH ₂) _n SO ₂ CH ₃ and CH ₂ (CH ₂) _n OCH ₃ , wherein the
	3	subscript n is an integer from 0 to 2.
	1	31. A compound of claim 29, wherein R ⁶ is
		or or .
	2	
	1	32. A compound of claim 29, wherein R ⁷ is selected from H, halogen,
c 10	2	CF_3 and (C_1-C_4) alkyl.
A	1	33. A compound of clarm 29, wherein R ⁷ is methyl.
•	1	34. A compound of claim 1, having the formula:
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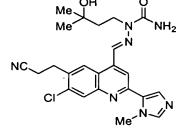
- wherein Y is O, S or N-CN; W' is N(CH₃), N(CF₃), N(CH₂CH₃), O or S; the subscripts n 3
- and n' are independently integers from 0 to 3; R⁷ is H, halogen, CF₃, CF₃O, (C₁-C₄)alkyl, 4
- (C₂-C₄)alkenyl, (C₂-C₄)alkynyl, (C₁-C₄)heteroalkyl or cyano; R⁹ is CN, CONH₂, CO-NH-5
- (C_1-C_6) alkyl, CO-N[(C_1-C_6) alkyl]₂, CO-NH- (C_1-C_6) heteroalkyl, CO-N[(C_1-C_6) alkyl) 6
- C₆)heteroalkyl]₂, S(O)_n"-(C₁-C₆)alkyl, S(O)_n"-(C₁-C₆)heteroalkyl, heteroaryl, (C₁-
- C₆)alkoxy or (C₃-C₆)cycloheteroalkyl, wherein each n" is independently an integer of 0 to
- 3 8 6 9 10 11 10 11 C_6)heteroalkyl, (C_1-C_6) heteroalkyl, $(O)_n$ - (C_1-C_6) alkyl, $S(O)_n$ - (C_1-C_6) heteroalkyl, aryl,
 - heteroaryl, O- $(C_1$ - $C_6)$ alkyl, O- $(C_1$ - $C_6)$ heteroalkyl or $(C_3$ - $C_8)$ cycloheteroalkyl; and R^{11} is
- 12° H, CF₃, NH₂, NH- (C_1-C_6) alkyl, N[(C_1-C_6) alkyl]₂, halogen or (C_1-C_3) alkyl.

1 1 2 2 3 3 A compound of claim 34, wherein Y is O or S; W' is N-CH₃; n is **35**.

- 2; n' is 1-3; R^9 is cyano, CONH₂, SO_2 -(C_1 - C_6)alkyl, (C_1 - C_6)alkoxy or (C_3 -
- C_6)cycloheteroalkyl; R^{10} is NH- $(C_1$ - C_6)alkyl, N_1 (C_1 - C_6)alkyl]₂, NH- $(C_1$ - C_6)heteroalkyl,
- $N[(C_1-C_6)heteroalkyl]_2$, $O-(C_1-C_6)alkyl$, $O-(C_1-C_6)heteroalkyl$, $(C_1-C_6)alkoxy$ or $(C_3-C_6)heteroalkyl]_2$ 4
- C₈)cycloheteroalkyl; and R¹¹ is H. 5
- A compound of claim 22, wherein B contains a nitrogen atom at a 1 **36**.
- position two atoms away from the atom attaching B to the remainder of the molecule. 2
- 1 **37**. A compound of claim 22, wherein B contains a nitrogen atom at
- the point of attachment of B to the remainder of the molecule. 2
- A compound of claim 22, wherein B is selected from the group **38**. 1
- consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted 2
- thiazolyl and substituted or unsubstituted triazolyl. 3
- A compound of claim 22, wherein B is selected from the group 1 **39**.
- consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol\5-yl, 5-methylimidazol-2



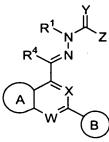
- 1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-3
- triazolyl, and 4-methyl-1,2,4-triazol-3-yl. 4
- A compound of claim 1, wherein Y is S; Z is NH_2 and R^1 is $(C_1$ -1 **40**.
- C₆)alkyl. 2
- A compound of claim 40, wherein R¹ is methyl. 41. 1
- 42. A compound of claim 1, wherein said compound is selected from the 1
- 2 group consisting of:



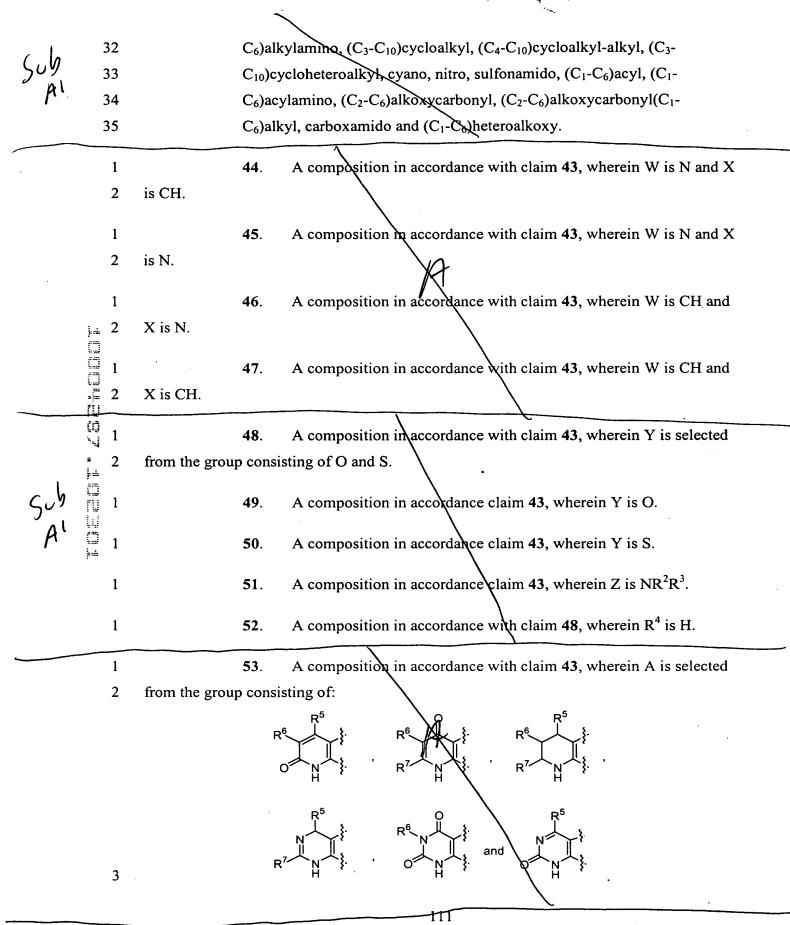
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3 4 wherein W and X are independently selected from the group consisting of N and CH; 5 6 Y is selected from the group consisting of O, S and N(R); 7 wherein R is selected from the group consisting of H, CN, NO₂, (C₁-8 C_{10})alkyl $\(C_3-C_{10})$ cycloalkyl, (C_4-C_{10}) cycloalkyl-alkyl, (C_3-C_{10}) C₁₀)alkeny and (C₂-C₁₀)alkynyl; 9 Z is selected from the group consisting of H, (C_1-C_{10}) alkyl, (C_3-C_{10}) cycloalkyl, 11 11 12 13 14 (C₄-C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³; R¹, R² and R³ are independently selected from the group consisting of H, (C₁- C_{10})alkyl, (C_3-C_{10}) alkenyl, (C_2-C_{10}) alkynyl, (C_2-C_{10}) heteroalkyl, (C_3-C_{10}) C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, (C_3-C_{10}) cycloheteroalkyl, aryl (C_1-C_4) alkyl, aryl (C_2-C_4) heteroalkyl, heteroaryl(C₂-C₄)alkyl, heteroaryl(C₂-C₄)heteroalkyl and perfluoro(C₁-<u>_</u> 16 C₆)alkyl; and wherein when Z is $\sqrt{R^2R^3}$, R^2 and R^3 can be combined to □ 18 form a 5- to 7-membered ring; and wherein when Y is N(R), R and R¹ are 19 optionally combined to form a 5- to \(\nabla\)-membered ring; R^4 is selected from the group consisting of H,\(C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, 20 (C_4-C_7) cycloalkyl-alkyl, (C_2-C_6) alkenyl\and (C_2-C_6) alkynyl; 21 A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system, 22 said ring system being mono- or bicyclic wherein said mono- or bicyclic 23 rings are selected from the group consisting of five- and six-membered 24 rings that are aromatic or partially or completely saturated; and 25 B is a substituted or unsubstituted five- or six-membered ring which is aromatic or 26 partially or completely saturated, containing at least one nitrogen atom, 27 and from 0 to 3 additional heteroatoms, wherein the B ring substituents are 28 selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl, 29 perfluoro(C_1 - C_6)alkyl, (C_2 - C_6)alkenyl, (C_2 - C_6)alkynyl, (C_1 - C_6)heteroalkyl, 30 (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-31



2 from the group consisting of

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wherein

R⁵, R⁶, R⁷ and R⁸ are independently selected from the group consisting of H, halogen, CF₃, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, cyano, nitro, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₂-C₆)alkoxycarbonyl, (C₃-C₆)alkoxycarbonylalkyl, CONH₂, CO-NH-(C₁-C₆)alkyl, CO-N[(C₁-C₆)alkyl, CO-N[(

 (C_3-C_6) alkoxycarbonylalkyl, CONH₂, CO-NH- (C_1-C_6) alkyl, CO-N[(C_1-C_6) alkyl]₂, SO₂NH₂, SO₂NH- (C_1-C_6) alkyl, SO₂N- $[(C_1-C_6)$ alkyl]₂ and (C_1-C_6) heteroalkoxy; or two adjacent R groups can be linked together to form

a new 5- or 6-membered carbocyclic or heterocyclic ring.

1 55. A composition in accordance with claim 43, wherein W is N; X is 2 CH; Y is O or S; and A is selected from the group consisting of:

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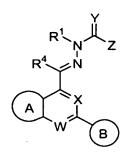
1 56. A composition in accordance with claim 43, wherein B contains a

2 nitrogen atom at a position two atoms away from the atom attaching B to the remainder of

3 the molecule.

1	57. A composition in accordance with claim 43, wherein B contains a
2	nitrogen atom at the point of attachment of B to the remainder of the molecule.
1	58. A composition in accordance with claim 43, wherein B is selected
2	from the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-
3	methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-
4	methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.
1	59. A composition in accordance with claim 43, wherein B is selected
2	from the group consisting of substituted or unsubstituted imidazolyl, substituted or
3	unsubstituted thiazolyl and substituted or unsubstituted triazolyl.
1	60. A composition in accordance with claim 55, wherein B contains a
2	nitrogen atom at a position two atoms away from the atom attaching B to the remainder of
3	the molecule.
1	61. A composition in accordance with claim 55, wherein B contains a
2	nitrogen atom at the point of attachment of B to the remainder of the molecule.
1	62. A composition in accordance with claim 55, wherein B is selected
2	from the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-
3	methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-
4	methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.
1	63. A composition in accordance with claim 55, wherein B is selected
2	from the group consisting of substituted or unsubstituted imidazolyl, substituted or
3	unsubstituted thiazolyl and substituted or unsubstituted triazolyl.
1	64. A method for treating an inflammatory, metabolic or malignant
2	condition, said method comprising administering to a subject in need of such treatment,

an effective amount of a compound having the formula;



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wherein

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W and X are independently selected from the group consisting of N and CH; Y is selected from the group consisting of O, S and N(R); wherein $\ R$ is selected from the group consisting of H, CN, NO₂, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃- C_{10})alkenyl and (C_2-C_{10}) alkynyl; Z is selected from the group consisting of H, (C_1-C_{10}) alkyl, (C_3-C_{10}) cycloalkyl, (C_4-C_{10}) cycloalkyl-alkyl, (C_2-C_{10}) alkenyl, (C_2-C_{10}) alkynyl and NR²R³; R¹, R² and R³ are independently selected from the group consisting of H, (C₁- C_{10})alkyl, (C_3-C_{10}) alkenyl, (C_2-C_{10}) alkynyl, (C_2-C_{10}) heteroalkyl, (C_3-C_{10}) C_{10})cycloalkyl, (C_4-C_{10}) cycloalkyl-alkyl, (C_3-C_{10}) cycloheteroalkyl-alkyl, (C_3-C_{10}) cycloheteroalkyl, aryl, aryl (C_1-C_4) alkyl, aryl (C_2-C_4) heteroalkyl, heteroaryl(C₂-C₄)alkyl, heteroaryl(C₂-C₄)heteroalkyl and perfluoro(C₁-C₆)alkyl; and wherein when Z is NR²R³, R² and R³ can be combined to form a 5- to 7-membered ring; and wherein when Y is N(R), R and R¹ are optionally combined to form a 5- to 7-membered ring; R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, (C_4-C_7) cycloalkyl-alkyl, (C_2-C_6) alkenyl and (C_2-C_6) alkynyl; A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system, said ring system being mono- or bicyclic wherein said mono- or bicyclic rings are selected from the group consisting of five- and six-membered rings that are aromatic or partially or dompletely saturated; and B is a substituted or unsubstituted five- or six-membered ring which is aromatic or partially or completely saturated, containing at least one nitrogen atom, and from 0 to 3 additional heteroatoms, wherein the B ring substituents are selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl, perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl,

 (C_1-C_6) alkoxy, (C_1-C_6) thioalkoxy, amino, $(C_1-\dot{C}_6)$ alkylamino, di $(C_1-\dot{C}_6)$ alkylamino, di $(C_1-\dot{C}_6)$ alkylamino, di

(b	33	C ₆)alkylamino, (C ₃ -C ₁₀)cycloalkyl, (C ₄ -C ₁₀)cycloalkyl-alkyl, (C ₃ -
20%	34	C ₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C ₁ -C ₆)acyl, (C ₁ -
H	35	C_6) acylamino, (C_2-C_6) alkoxycarbonyl, (C_2-C_6) alkoxycarbonyl (C_1-C_6)
	36	C ₆)alkyl, carboxamido and (C ₁ C ₆)heteroalkoxy.
	1	65. A method in accordance with claim 64, wherein W is N and X is
	2	CH.
	1	66. A method in accordance with claim 64, wherein W is N and X is N.
	1	67. A method in accordance with claim 64, wherein W is CH and X is
	2	N.
	<u>i</u> 1	68. A method in accordance with claim 64, wherein W is CH and X is
	2	CH.
		69. A method in accordance with claim 65, wherein Y is selected from
. 1.		the group consisting of O and S.
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•		71. A method in accordance with claim 65, wherein Y is S.
	1	72. A method in accordance with claim 65, wherein Z is NR ² R ³ .
	1	73. A method in accordance with claim 69, wherein R ⁴ is H.
	1	74. A method in accordance with claim 64, wherein A is selected from
	2	the group consisting of:
		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
	3	\mathbb{R}^{5} \mathbb{R}^{6} \mathbb{R}^{6} \mathbb{R}^{5} \mathbb{R}^{6} \mathbb{R}^{5} \mathbb{R}^{6} \mathbb{R}^{5} \mathbb{R}^{5} \mathbb{R}^{5}

wherein

R⁵, R⁶, R⁷ and R⁸ are independently selected from the group consisting of H, halogen, CF₃, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, cyano, nitro, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₂-C₆)alkoxycarbonyl, (C₃-C₆)alkoxycarbonylakyl, CONH₂, CO-NH-(C₁-C₆)alkyl, CO-N[(C₁-C₆)alkyl]₂, SO₂NH₂, SO₂NH-(C₁-C₆)alkyl, SO₂N-[(C₁-C₆)alkyl]₂ and (C₁-C₆)alkyl]₂ and (C₁-C₆)alkyl]₂ and (C₁-C₆)alkyl, SO₂N-[(C₁-C₆)alkyl]₂ and (C₁-C₆)alkyl)

C₆)heteroalkoxy; or two adjacent R groups can be linked together to form

76. A method in accordance with claim 64, wherein W is N; X is CH;
Y is O or S; and A is selected from the group consisting of:

a new 5- or 6-membered carbocyclic or heterocyclic ring.

$$R^{6}$$
 R^{7}
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 R^{8}

77. A method in accordance with claim 64, wherein B contains a

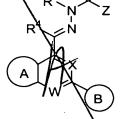
- 2 nitrogen atom at a position two atoms away from the atom attaching B to the remainder of
- 3 the molecule.

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1	78. A method in accordance with claim 64, wherein B contains a
2	nitrogen atom at the point of attachment of B to the remainder of the molecule.
	70 A static and the state of the CA subspace P is releated from
1	79. A method in accordance with claim 64, wherein B is selected from
2	the group consisting of -methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-
3	methylimidazol-1-yl, 5-(thifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-
4	methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.
1	80. A method in accordance with claim 64, wherein B is selected from
2	the group consisting of substituted or unsubstituted imidazolyl, substituted or
3	unsubstituted thiazolyl and substituted or unsubstituted triazolyl.
1	81. A method in accordance with claim 76, wherein B contains a
1	\
2	nitrogen atom at a position two atoms away from the atom attaching B to the remainder of
3	the molecule.
1	82. A method in accordance with claim 76, wherein B contains a
2	nitrogen atom at the point of attachment of B to the remainder of the molecule.
1	83. A method in accordance with claim 76, wherein B is selected from
2	the group consisting of 1-methylimidazol-5-yl, \1-(trifluoromethyl)imidazol-5-yl, 5-
3	methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-
4	methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-8-yl.
_	
1	84. A method in accordance with claim 76, wherein B is selected from
2	the group consisting of substituted or unsubstituted imidazolyl, substituted or
3	unsubstituted thiazolyl and substituted or unsubstituted triazolyl.
1	85. A method in accordance with claim 64, wherein said compound is
2	administered orally.
۷	administered drafty.
1	86. A method in accordance with claim 64, wherein said compound is
2	administered topically.
1	87. A method in accordance with claim 64, wherein said compound is
2	administered intravenously or intramuscularly.

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1	88. A method in accordance with claim 64, wherein said compound is
2	administered in combination with a second therapeutic agent, said second therapeutic
3	agent being a member selected from the group consisting of prednisone, dexamethasone,
4	beclomethasone, methylprednisone, betamethasone, hydrocortisone, methotrexate,
5	cyclosporin, rapamycin, tacrolimus, antihistamine drugs, TNF antibodies, IL-1 antibodies
6	soluble TNF receptors, soluble IL-1 receptors, TNF or IL-1 receptor antagonists, non-
7	steroidal antiinflammatory agents, COX-2 inhibitors, antidiabetic agents, and anticancer
8	agents.
1	89. A method in accordance with claim 88, wherein said administering
2	is sequential.
1	90. A method in accordance with claim 64, wherein said inflammatory
2	metabolic or malignant condition is selected from the group consisting of rheumatoid
3	arthritis, inflammatory bowel disease, psoriasis, cancer, diabetes and septic shock.
1	91. A method for treating a condition or disorder mediated by IKK,
2	comprising
3	administering to a subject in need thereof a therapeutically effective
4	amount of a compound having the formula:
	\mathbb{R}^{1} \mathbb{N} \mathbb{Z}
	A
5	VV (B)
6	wherein
7	W and X are independently selected from the group consisting of N and CH;
8	Y is selected from the group consisting of O, s and N(R);
9	wherein R is selected from the group consisting of H, CN, NO ₂ , (C ₁ -
10	C_{10})alkyl, (C_3 - C_{10})cycloalkyl, (C_4 - C_{10})cycloalkyl-alkyl, (C_3 -
11	C_{10})alkenyl and (C_2 - C_{10})alkynyl; \setminus
12	Z is selected from the group consisting of H, $(C_1 - c_{10})$ alkyl, $(C_3 - C_{10})$ cycloalkyl,
13	(C_4-C_{10}) cycloalkyl-alkyl, (C_2-C_{10}) alkenyl, (c_2-C_{10}) alkynyl and NR^2R^3 ;

		1
	14	R ¹ , R ² and R ³ are independently selected from the group consisting of H, (C ₁ -
	15	C_{10})alkyl, (C_3 - C_{10})alkenyl, (C_2 - C_{10})alkynyl, (C_1 - C_{10})heteroalkyl, (C_3 -
	16	C_{10})cycloalkyl, (C ₄ -C ₁₀)cycloalkyl-alkyl, (C ₃ -C ₁₀)cycloheteroalkyl-alkyl,
	17	(C_3-C_{10}) cycloheteroalkyl, aryl, aryl (C_1-C_4) alkyl, aryl (C_1-C_4) heteroalkyl,
	18	heteroaryl(C_1 - C_4)alkyl, heteroaryl(C_1 - C_4)heteroalkyl and perfluoro(C_1 -
	19	C ₆)alkyl; and wherein when Z is NR ² R ³ , R ² and R ³ can be combined to
	20	form a 5- to 7-membered heterocyclyl ring;
و ال	21	R ⁴ is selected from the group consisting of H, (C ₁ -C ₆)alkyl, (C ₃ -C ₆)cycloalkyl,
Al	22	(C ₄ -C ₇)cycloalkyl-alkyl, (C ₂ -C ₆)alkenyl and (C ₂ -C ₆)alkynyl;
,	23	A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,
_	24	said ring system being mono- or bicyclic wherein said mono- or bicyclic
	25	rings are selected from the group consisting of five- and six-membered
	26	rings that are aromatic or partially or completely saturated; and
	27	B is a substituted or unsubstituted five- or six-membered ring which is aromatic or
the day	28	partially or completely saturated, containing at least one nitrogen atom,
	29	and from 0 to 3 additional heteroatoms, wherein th 2 ring substituents are
to men dank dank men legi men	30	selected from the group consisting of halogen, CF ₃ , CF ₃ O, (C ₁ -C ₆)alkyl,
	31	perfluoro(C_1 - C_6)alkyl, (C_2 - C_6)alkenyl, (C_2 - C_6)alkynyl, (C_1 - C_6)heteroalkyl,
	32	(C_1-C_6) alkoxy, (C_1-C_6) thioalkoxy, amino, (C_1-C_6) alkylamino, di (C_1-C_6)
[] }=	33	C_6)alkylamino, (C_3 - C_{10})cycloalkyl, (C_4 - C_{10})cycloalkyl-alkyl, (C_3 -
	34	C_{10})cycloheteroalkyl, cyano, nitro, sulfonamido, $(C_1 - C_6)$ acyl, $(C_1 - C_6)$
	35	C_6)acylamino, (C_1 - C_6)alkoxycarbonyl, (C_1 - C_6)alkoxycarbonyl(C_1 -
	36	C_6)alkyl, carboxamido and (C_1-C_6) heteroalkoxy.
	1	92. A method for modulating IKK, comprising
	. 1	\
	2	contacting a cell with a compound having the formula:
		\ R¹ \



4 wherein

3

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W and X are independently selected from the group consisting of N and CH;

6	Y is selected from the group consisting of O, S and $N(R)$;
7	wherein R is selected from the group consisting of H, CN, NO ₂ , (C ₁ -
8	C_{10})alkyl, (C_3 - C_{10})cycloalkyl, (C_4 - C_{10})cycloalkyl-alkyl, (C_3 -
9	\setminus C ₁₀)alkenyl and (C ₂ -C ₁₀)alkynyl;
10	Z is selected from the group consisting of H, (C ₁ -C ₁₀)alkyl, (C ₃ -C ₁₀)cycloalkyl,
11	(C_4-C_{10}) cycloalkyl-alkyl, (C_2-C_{10}) alkenyl, (C_2-C_{10}) alkynyl and NR^2R^3 ;
12	R^1 , R^2 and R^3 are independently selected from the group consisting of H, (C ₁ -
13	C_{10})alkyl, (C_3 - C_{10})alkenyl, (C_2 - C_{10})alkynyl, (C_1 - C_{10})heteroalkyl, (C_3 -
14	C_{10})cycloalkyl, (C_4 - C_{10})cycloalkyl-alkyl, (C_3 - C_{10})cycloheteroalkyl-alkyl,
15	(C_3-C_{10}) cycloheteroalkyl, aryl, aryl (C_1-C_4) alkyl, aryl (C_1-C_4) heteroalkyl,
16	heteroaryl(C_1 - C_4)alkyl, heteroaryl(C_1 - C_4)heteroalkyl and perfluoro(C_1 -
17	C ₆)alkyl; and wherein when Z is NR ² R ³ , R ² and R ³ can be combined to
18	form a 5- to 7-membered heterocyclyl ring;
19	R ⁴ is selected from the group consisting of H, (C ₁ -C ₆)alkyl, (C ₃ -C ₆)cycloalkyl,
20	(C_4-C_7) cycloalkyl-alkyl, (C_2-C_6) alkenyl and (C_2-C_6) alkynyl;
21	A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,
22	said ring system being mono- or bicyclic wherein said mono- or bicyclic
23	rings are selected from the group consisting of five- and six-membered
24	rings that are aromatic or partially or completely saturated; and
25	B is a substituted or unsubstituted five- or six-membered ring which is aromatic or
26	partially or completely saturated, containing at least one nitrogen atom,
27	and from 0 to 3 additional heteroatoms, wherein the B ring substituents are
28	selected from the group consisting of halogen, CF ₃ , CF ₃ O, (C ₁ -C ₆)alkyl,
29	perfluoro(C_1 - C_6)alkyl, (C_2 - C_6)alkenyl, (C_2 - C_6)alkynyl, (C_1 - C_6)heteroalkyl,
30	(C_1-C_6) alkoxy, (C_1-C_6) thioalkoxy, amino, (C_1-C_6) alkylamino, di (C_1-C_6)
31	C_6) alkylamino, (C_3-C_{10}) cycloalkyl, (C_4-C_{10}) cycloalkyl-alkyl, (C_3-C_{10})
32	C_{10})cycloheteroalkyl, cyano, nitro, sulfonamido, (C_1 - C_6)acyl, (C_1 -
33	C_6)acylamino, (C_1 - C_6)alkoxycarbonyl, (C_1 - C_6)alkoxycarbonyl(C_1 -
34	C_6)alkyl, carboxamido and (C_1 - C_6)heteroalkoxy.
1	93. The method of Claim 92, wherein said compound is an IKK
2	inhibitor.

4 activator.

3

- 1 95. A method for the preparation of antiinflammation agents
- 2 comprising contacting a precursor compound having the formula:

4 wherein

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W and X are independently selected from the group consisting of N and CH; R^4 is selected from the group consisting of H, (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl,

(C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;

A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system, said ring system being mono- or bicyclic wherein said mono- or bicyclic rings are selected from the group consisting of five- and six-membered rings that are aromatic or partially or completely saturated; and

B is a substituted or unsubstituted five- or six-membered ring which is aromatic or partially or completely saturated, containing at least one nitrogen atom, and from 0 to 3 additional neteroatoms, wherein the B ring substituents are selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl, perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C₁-C₆)acyl, (C₁-

 C_6) acylamino, (C_2-C_6) alkoxycarbonyl, (C_2-C_6) alkoxycarbonyl (C_1-C_6)

 C_6)alkyl, carboxamido and (C_1-C_6) heteroalkoxy

with a compound having the formula:

$$R^1$$
 N Z

23

25

24 wherein

Y is selected from the group consisting of O, S and N(R);

26	wherein R is selected from the group consisting of H, Cin, NO_2 , (C ₁ -
27	C_{10})alkyl, (C_3 - C_{10})cycloalkyl, (C_4 - C_{10})cycloalkyl-alkyl, (C_3 -
28	C_{10}) alkenyl and (C_2-C_{10}) alkynyl;
29	Z is selected from the group consisting of H, (C ₁ -C ₁₀)alkyl, (C ₃ -C ₁₀)cycloalkyl,
30	$(C_4 \ C_{10})$ cycloalkyl-alkyl, $(C_2 - C_{10})$ alkenyl, $(C_2 - C_{10})$ alkynyl and NR^2R^3 ;
31	R^1 , R^2 and R^3 are independently selected from the group consisting of H, (C ₁ -
32	C_{10}) alkyl, (C_3-C_{10}) alkenyl, (C_2-C_{10}) alkynyl, (C_2-C_{10}) heteroalkyl, (C_3-C_{10})
33	C ₁₀)cycloalkyl, (C ₄ -C ₁₀)cycloalkyl-alkyl, (C ₃ -C ₁₀)cycloheteroalkyl-alkyl,
34	(C_3-C_{10}) cycloheteroalkyl, aryl, aryl (C_1-C_4) alkyl, aryl (C_2-C_4) heteroalkyl,
35	heteroaryl(C_{ξ} - C_4)alkyl, heteroaryl(C_2 - C_4)heteroalkyl and perfluoro(C_1 -
36	C ₆)alkyl; and wherein when Z is NR ² R ³ , R ² and R ³ can be combined to
37	form a 5- to 7-membered ring; and wherein when Y is N(R), R and R ¹ are
<u>₩</u> 38	optionally combined to form a 5- to 7-membered ring;
ີ່ 39	under conditions sufficient to produce compounds having the formula:
4 38 39	R^1 N Z R^4 N Z
140 140	A X B B D D D D D D D D D D D D D D D D D
41 =	wherein each of A, B, R^1 , R^4 , W, X, Y and Z have the meanings provided above.
1	96. A compound having the formula:

wherein

W and X are independently selected from the group consisting of N and CH;

R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl,

(C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;

A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system, said ring system being mono- or bicyclic wherein said mono- or bicyclic

9	rings are selected from the group consisting of five- and six-membered
10	rings that are aromatic or partially or completely saturated; and
11	B is a substituted or unsubstituted five- or six-membered ring which is aromatic or
12	partially or completely saturated, containing at least one nitrogen atom,
13	and from 0 to 3 additional heteroatoms, wherein the B ring substituents are
14	selected from the group consisting of halogen, CF ₃ , CF ₃ O, (C ₁ -C ₆)alkyl,
15	perfluoro(C_1 C_6)alkyl, (C_2 - C_6)alkenyl, (C_2 - C_6)alkynyl, (C_1 - C_6)heteroalkyl,
16	(C_1-C_6) alkoxy, (C_1-C_6) thioalkoxy, amino, (C_1-C_6) alkylamino, di (C_1-C_6)
17	C_6) alkylamino, $(\overset{\circ}{C_3}$ - C_{10}) cycloalkyl, $(C_4$ - C_{10}) cycloalkyl-alkyl, $(C_3$ -
18	C ₁₀)cycloheteroalky, cyano, nitro, sulfonamido, (C ₁ -C ₆)acyl, (C ₁ -
19	C_6) acylamino, (C_2-C_6) alkoxycarbonyl, (C_2-C_6) alkoxycarbonyl (C_1-C_6) (C_1-C_6) alkoxycarbonyl (C_1-C_6)
<u>-</u> 420	C_6)alkyl, carboxamido and (C_1-C_6) heteroalkoxy.
5 5 1 1 1 1 1 2	97. A compound of claim 96, wherein R ⁴ is hydrogen.
1 1 1 1	98. A compound of claim wherein R ⁴ is hydrogen, Y is O or S, and
-	$Z ext{ is } NR^2R^3$.
1	99. A compound of claim 96, wherein R ⁴ is hydrogen, Y is O or S, Z is
2	NR ² R ³ , and B contains a nitrogen atom at a position two atoms away from the atom
1 2 3	attaching B to the remainder of the molecule.
1	100. A compound of claim 96, B contains a nitrogen atom at the point of
2	attachment of B to the remainder of the molecule.
1	101. A compound of claim 99, wherein B is selected from the group
2	consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-
3	1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-
4	triazolyl, and 4-methyl-1,2,4-triazol-3-yl.